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(54) **Device for conducting chemical reaction sequences**

(57) A device for conducting chemical reaction sequences comprises a support (12) with a multiple number of positioning planes (I-III) and a multiple number of positioning regions (a, b, c) in the different positioning planes (I-III); in at least one of the positioning planes (I, II, III) a reaction vessel sliding support (20, 22) is provided, which supports a reaction vessel (34). This at least one reaction vessel (34) can be arranged in a transfer positioning region (T), wherein a reaction vessel (34) of a directly adjacent positioning plane (I, II, III) can be assigned to it for the selective transfer of reagents between these reaction vessels (34).

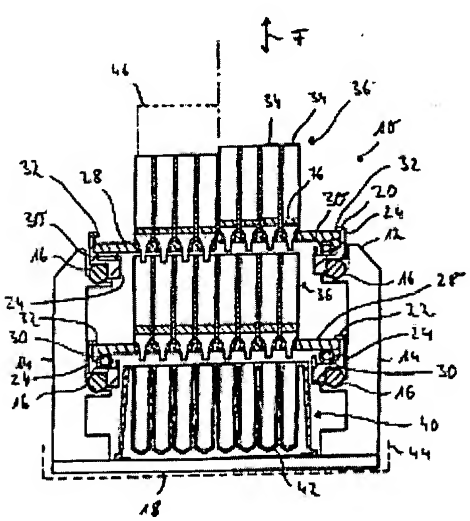

Fig. 2

Description

[0001] The present invention concerns a device for conducting chemical reaction sequences.

[0002] In many chemical or biochemical methods, which are conducted in several steps, it may be necessary to change the reaction medium, e.g., to change between a polar solvent and a nonpolar solvent. It may also be necessary to separate reaction products or reaction byproducts in a reaction step. For this purpose, conventional precipitation, filtration, centrifugation and drying of materials are used. In particular, it is often desired in the case of such reaction sequences to conduct a plurality of such reactions in parallel, in order to be able to simultaneously investigate several different initial materials, for example, or to be able to obtain statistical information on materials to be investigated or reaction courses by the distribution of different reaction results.

[0003] A device for conducting chemical reaction sequences is known from EP-0 365,668, with which several biochemical reactions can be conducted simultaneously, such as, for example, the synthesis of DNA fragments. This known device is comprised of a multiple number of plate elements arranged one above the other, wherein a reaction chamber as well as a multiple number of passage channels in line with the reaction chamber are disposed in each plate element. By lateral displacement of the respective plate elements, it is possible to bring the reaction chamber of one plate element into vertical alignment either with the reaction chamber of other plate elements

or with the passage channels of other plate elements. A site of introduction for introducing the bases A, C, G and T as well as an organic solvent is arranged above the plates. It is thus possible by suitable positioning to introduce one of the bases or the solvent into each reaction chamber of the different parts of the plate. In addition, each reaction chamber is constructed in such a way that it can be penetrated downward and is sealed by a porous membrane, so that glass beads on which reactions occur are retained in the individual reaction chambers, but a liquid introduced on top can pass downward. The same reaction will now be conducted simultaneously with the same base in all or several reaction chambers by means of this known device, and thus these reaction chambers, as has already been discussed, can be arranged in vertical alignment under the respective site of introduction. If such an arrangement is encountered, then the base will be introduced subsequently so that it enters into the reaction chamber arranged uppermost, passes through the porous membrane, and enters into the next reaction chamber lying thereunder, etc. The problem consists of the fact that reactions have already occurred in the reaction chambers arranged above as soon as the base is introduced and that the reaction products are entrained by the liquid that passes through them into the reaction chambers lying thereunder. In many processes, e.g., oligonucleotide synthesis, this leakage of reaction products is unimportant. When purifying biological material such as, e.g., DNA, however, this would make the reaction results useless.

[0004] It is thus the object of the present invention to provide a device for conducting chemical reaction sequences with which parallel reactions can be conducted in a simple way without the danger of mutual adverse effects due to reactions conducted

simultaneously. According to the invention, this object is solved by a device for conducting chemical reaction sequences, which comprises: a support with a multiple number of positioning planes, which are arranged successively in the direction of flow and substantially parallel to one another, wherein each positioning plane comprises a multiple number of positioning regions lying next to one another substantially orthogonal to the direction of flow and wherein relative to at least one positioning region in one of the positioning planes, a positioning region aligned in the direction of flow to this is present in at least one directly adjacent positioning plane, [and] in at least one of the positioning planes [there is] at least one reaction vessel sliding support with at least one reaction vessel, wherein the reaction vessel sliding support can be moved in the assigned positioning plane, so that the at least one reaction vessel or at least one part of the reaction vessel borne on the reaction vessel sliding support can be arranged in at least one transfer positioning region, wherein one reaction vessel of a directly adjacent positioning plane can be assigned to each reaction vessel arranged in the at least one transfer positioning region for the selective transfer of reagents between these reaction vessels.

[0005] It is provided in the device according to the invention that in each positioning plane at least one reaction vessel is provided, and that a change of reagents between the individual planes can occur due to the movement of the reaction vessel sliding supports of different positioning planes into suitable transfer positioning regions. This means that one processing channel, which is provided exclusively for one sample, is provided for each processed sample in the direction of flow. A leakage of reaction products from one processing channel into another one thus cannot occur. This has the

consequence that even highly sensitive reactions can be conducted in large number parallel to one another without mutual adverse effects. By the suitable selection of the number of positioning planes, it is possible to conduct reaction sequences which involve any desired number of reaction steps, wherein only relatively little laboratory space is required for the parallel conducting of even a large number of positioning planes, due to the stacked arrangement of the positioning planes.

[0006] It is indicated that in the present text the term "reagents" includes any material which can be used as a catalyst or the like, on the one hand, for carrying out or promoting reactions. On the other hand, this expression also includes reaction products, byproducts or the like, which are to be eliminated either as reaction waste or are processed further in additional reaction steps.

[0007] In a particularly advantageous configuration of the device according to the invention, it is provided that the at least one reaction vessel sliding support bears at least one row of reaction vessels, in which at least one reaction vessel is arranged. The row-like arrangement of reaction vessels makes possible a particularly simple and space-saving execution of several reactions parallel to one another.

[0008] It is thus advantageous if the at least one row of reaction vessels is supported on the at least one reaction vessel sliding support by a reaction vessel support assigned to this row.

[0009] In the device according to the invention, the reaction vessel sliding supports can be moved in the individual positioning planes, i.e., the reaction vessel sliding supports of

different planes can be moved relative to one another. This means that an intermediate space must be created in the positioning regions of the reaction vessel sliding supports of positioning planes directly adjacent to one another in the direction of flow, in order to make possible such free mobility. However, for the transfer of reagents between directly adjacent positioning planes, in order to be able to assure that the reaction vessels between which a transfer of reagents will occur lie as closely together as possible, it is proposed that each reaction vessel borne on the at least one reaction vessel sliding support, for the transfer of reagents between this vessel and an assigned reaction vessel each time in a directly adjacent positioning plane in the direction of flow, can be moved onto the assigned reaction vessel of the directly adjacent positioning plane. Thus the danger of an unintentional spilling of reagents into the environment can be clearly reduced.

[0010] In order to be able to achieve such a bringing together of reaction vessels of directly adjacent positioning planes, it can be provided, for example, that the reaction vessel support bearing the at least one row of reaction vessels is arranged so that it can be moved up and down on the at least one reaction vessel sliding support in the direction of flow. A multiple number of reaction vessels can therefore be moved up and down by the movement of the reaction vessel support, so that independent movement means need not be provided for individual reaction vessels.

[0011] Advantageously, movement means are then provided for executing the up-and-down movement of the reaction vessel support.

[0012] The movement means can be designed, for example, for exercising a pressure force on each reaction vessel supported on the reaction vessel support, wherein, when exercising the pressure force, each reaction vessel can be moved with the reaction vessel support against a prestressing force onto the reaction vessel of the directly adjacent positioning plane assigned each time.

[0013] In a particularly simple way, the prestressing force can be produced by prestressing means acting between the at least one reaction vessel sliding support and the reaction vessel support, preferably spring means, elastically deformable plastic elements or the like.

[0014] Alternatively, it is possible, however, that displacement means are provided, which act directly between the at least one reaction vessel sliding support and the reaction vessel support.

[0015] In order to be able to further control the unintentional release of reagents into the environment, which has been mentioned previously, or to be able to completely suppress it, it is proposed that sealing means are provided, which, in a state of reaction vessels where two directly adjacent positioning planes are moved toward one another, produce a substantially fluid-tight seal between the reaction vessels of the different positioning planes allocated to one another each time.

[0016] According to a particularly advantageous configuration, it can be provided that the sealing means comprise an essentially point-shaped outlet end of the at least one reaction vessel of one positioning plane, as well as a receiving end, which is sealed by

membrane means, of the respectively assigned reaction vessel of the other positioning plane, wherein, when the reaction vessels of the different positioning planes on opposite sides approach one another, the membrane means can be penetrated by the pointed outlet ends and form a fluid-tight seal with these pointed ends.

[0017] Alternatively, it is possible that the sealing means comprise a layer of sealing material on one side of the reaction vessel support, which is turned toward the assigned reaction vessels of the directly adjacent positioning plane, wherein when the reaction vessel support moves onto the reaction vessels of the directly adjacent positioning plane, the sealing material layer at the receiving ends of the reaction vessels of the directly adjacent positioning plane is applied and forms by these ends a fluid-tight seal.

[0018] In order to provide a venting or aerating of the reaction vessels, when the fluid-tight seal is produced between two reaction vessels between which a transfer of reagents will occur, in particular, those reaction vessels, in which fluid is supplied, it is proposed that additional venting means are provided, which make possible an aeration or venting of the reaction vessels when there is a fluid-tight connection of the reaction vessels of two directly adjacent positioning planes.

[0019] For example, it can be provided that the venting means comprise venting channel means, which extend away from the outlet ends of the reaction vessels, preferably inside the respective reaction vessels, and preferably are open to the environment via filtering means. With such a configuration, the venting means are provided directly in the reaction vessels, so that no external venting devices need to be

provided, which leads to a particularly simple construction of the device according to the invention.

[0020] Alternatively it is also possible that the at least one reaction vessel is supported on the allocated reaction vessel support in the region of its outlet end, and that the venting means provided on the reaction vessel support, passing through the support and the layer of sealing material approximately in the direction of flow and the outlet end of the at least one reaction vessel comprise surrounding or ambient venting channel means, which, when the reaction vessel support is applied on the receiving ends of the assigned reaction vessels of the directly adjacent positioning plane produce a connection for the flow of gas between the inside space of each assigned reaction vessel of the directly adjacent positioning plane and the environment, preferably via filtering means.

[0021] When liquid reagents are introduced into the reaction vessels, in order to prevent these reagents from immediately flowing out again from the outlet regions of the reaction vessels, it is proposed that additional sealing means, preferably filtering means are provided in the at least one reaction vessel, preferably in the region of the outlet end, and these sealing means make possible a passage of fluid only when an external action is applied.

[0022] For example, the external action can result in the application of a pressure or of an underpressure on the inside of the reaction vessels, or can be an electrical, magnetic or gravitational action.

[0023] In order to be able to introduce reagents into the reaction vessels or to be able to remove reagents, i.e., reaction products and byproducts from the reaction vessels, and, for example, to be able to transfer them again into a positioning plane that lies on top, it is proposed that means for introducing and removing reagents are further provided for introducing reagents into the at least one reaction vessel in at least one of the positioning planes or for removing reagents from the at least one reaction vessel of at least one of the positioning planes.

[0024] In order also to be able to avoid here the unintentional spilling of reagents into the environment, it is proposed that the means for introducing and removing reagents can be connected in a fluid-tight manner with the respective reaction vessels in order to introduce and remove reagents.

[0025] In order to be able to take care of each positioning plane, i.e. the reaction vessels arranged in the latter, via the means for introducing and removing reagents, it is proposed that each positioning plane comprises at least one introduction/removal positioning region, wherein during the positioning of at least one part of the reaction vessels provided in one positioning plane in the at least one introduction/removal positioning region, these reaction vessels are freely accessible from one side to the means for introducing and removing reagents, preferably from the upper side, for introducing reagents into these vessels and removing them therefrom in the direction of flow.

[0026] According to a particularly advantageous configuration, it may be provided that the means for introducing and removing reagents additionally form movement means,

which produce the pressure force on the reaction vessels for moving the vessels in the direction of flow.

[0027] According to one configuration, it can be provided that the reaction vessel sliding supports can be moved linearly in each of the assigned positioning planes. Alternatively, it is possible, however, to move the reaction vessel sliding supports into the allocated positioning planes on approximately circular tracks. This means that, on the one hand, the device according to the invention has a linear construction and, in the second embodiment, has an approximately rotationally symmetric construction, wherein the reaction vessel sliding supports in the individual positioning planes can then be rotated around a central axis.

[0028] In order to be able to provide a nearly automatic carrying out of reactions or reaction sequences, it is proposed that means are provided for effecting the movement of the reaction vessel sliding supports into the assigned positioning planes.

[0029] According to a particularly advantageous configuration, it can then be provided in turn that the means for introducing and removing reagents form the means for executing the movement of the reaction vessel sliding supports into the allocated positioning planes.

[0030] In order to be able to collect the reaction products at the end of the respective reaction sequences, it is proposed that the at least one reaction vessel in one of the positioning planes, preferably of the last positioning plane in the direction of flow, is a

collecting vessel for the uptake of the reaction products produced by the chemical reactions.

[0031] It may be necessary in different steps to remove the liquid reagents present in the reaction vessels as reaction byproducts or wastes and to further utilize only the reagents contained, for example, in certain substrates. Therefore, it is advantageous if collecting tank means are subsequently provided on the last positioning plane in the direction of flow, into which these liquid reaction byproducts can then be washed out.

[0032] In particular, when a plurality of positioning planes are provided, it is advantageous to provide that at least some of the positioning planes comprise an uptake positioning region and others comprise an output positioning region, that the uptake positioning region of such a positioning plane is aligned in the direction of flow with the output positioning region of a preceding positioning plane in the direction of flow, and/or that the output positioning region of such a positioning plane is aligned in the direction of flow with the uptake positioning region of a successive positioning plane in the direction of flow. Since a transfer of reagents occurs only between directly adjacent positioning planes, it therefore suffices to provide an uptake positioning region and an output positioning region in each positioning plane, wherein, however, for example, positioning regions can also be provided, which define intermediate positions.

[0033] Since the first positioning plane for the means for introducing and removing reagents in the direction of flow is always freely accessible, it can be provided that at least the first positioning plane in the direction of flow comprises an uptake/output positioning region, which forms both the uptake positioning region as well as also the

output positioning region. In a corresponding manner, it is sufficient if the last positioning plane in the direction of flow comprises only uptake positioning regions, preferably one uptake positioning region.

[0034] In order to assure the ability to freely position the respective reaction vessel sliding supports in each of the positioning regions provided for them, it is proposed that the positioning regions of the different positioning planes are disposed in such a way that they can be arranged relative to their respective positioning region in each positioning plane in such a way, that each reaction vessel sliding support can be arranged in any other positioning plane, preferably via the means for introducing and removing reagents, with its (their) allocated reaction vessel(s) in each of the positioning regions provided for these reaction vessels.

[0035] For example, such an arrangement may be encountered that the uptake and output positioning regions of the different positioning planes are disposed in a step-like structure, wherein at least a part of each output positioning region is not covered by a positioning region of a preceding positioning plane in the direction of flow. This arrangement leads to the fact that in each positioning plane a region is provided, in which the reaction vessels disposed in this positioning plane are freely accessible, for example, from the top, to the means for introducing and removing reagents, on the one hand, for the introduction and removal of reagents, and on the other hand, for conducting the displacement of the allocated reaction vessel sliding support.

[0036] The present invention further concerns a method for conducting chemical reaction sequences, comprising the steps:

a) Introducing reagents into the at least one reaction vessel of a first positioning plane,

b) Conducting a chemical reaction, an adsorption reaction, an adsorption reaction of a substance mixture or the like, in the at least one reaction vessel,

c) Arranging the at least one reaction vessel of the first positioning plane and the reaction vessel allocated each time of a second positioning plane directly following the first positioning plane in a transfer positioning region of the two positioning planes,

d) Controlled transferring of at least one part of the reaction products obtained in step b) into each allocated reaction vessel of the second positioning plane, whereby the at least one reaction vessel of the first positioning plane or/and the reaction vessel of the second positioning plane allocated each time can be positioned in such a way that the at least one reaction vessel in the second positioning plane is freely accessible for the introduction of reagents into it via the means for introducing and removing reagents or/and is positioned for the controlled transfer of reaction products contained in it into an allocated reaction vessel each time of a third positioning plane which follows the second positioning plane.

[0037] The device according to the invention is described in detail below on the basis of preferred embodiments referred to the attached drawings. Here:

Fig. 1 shows a schematic lateral view of a device according to the invention for conducting chemical reaction sequences;

Fig. 2 shows a sectional view along a line II-II in Fig. 1, wherein, however, reaction vessels or collecting vessels are shown in each positioning plane and wherein some of the reaction vessels shown in the uppermost positioning plane are in a lowered state;

Fig. 3 shows a top view onto a reaction vessel sliding support of the device according to the invention;

Fig. 4 shows a lateral view of a dispenser tool partially cut away along a line IV-IV in Fig. 5;

Fig. 5 shows a sectional view of the dispenser tool along a line V-V in Fig. 4;

Fig. 6 shows a partial sectional view of an embodiment of reaction vessels supported on a reaction vessel support;

Fig. 7 shows a partial sectional view of an alternative embodiment of reaction vessels supported on a reaction vessel support along a line VII-VII in Fig. 8;

Fig. 8 shows a top view onto the reaction vessel support of Fig. 7; and

Fig. 9 shows a sketched representation of an embodiment of the device according to the invention with five positioning planes.

[0038] Figs. 1 and 2 show a device generally denoted 10 for conducting reaction sequences. Device 10 comprises a support 12, which defines a multiple number of positioning planes I, II and III arranged on top of one another as well as a multiple number of positioning regions a, b, c. Support 12 has vertical long walls 14, which are

disposed in a row successively on both sides of support 12 and which are joined together in a longitudinal direction by horizontal long walls 16 or possibly a frame-shaped bottom plate 18. The vertical long walls 14 and the horizontal long walls 16 or the bottom plate 18 are joined solidly with one another by suitable means, such as, e.g., screws or the like.

[0039] The horizontal long walls 16 form guide rails each time for reaction vessel sliding supports 20, 22, wherein the reaction vessel sliding support 20 is disposed in plane I and the reaction vessel sliding support 22 is disposed in plane II.

[0040] As can also be recognized in Fig. 3, each reaction vessel sliding support comprises lateral guide parts 24, which are joined solidly with one another by connecting parts 26 at respective end regions. The guide parts 24 and the connecting parts 26 thus form a rigid frame for the reaction vessel sliding support 20 or 22. The reaction vessel sliding supports 20 and 22 can be freely moved by guide parts 24 on the respective horizontal long walls 16 in the positioning planes I, II. For this purpose, sliding or roller bearing means or the like, which are not shown in the figure, can be provided between the guide parts 24 and the horizontal long walls 26*. Further, in order to be able to attach the guide slide supports in the respective positioning regions, the reaction vessel sliding supports 20, 22 can be formed so that they are self-braking or specific catching or fastening elements can be provided, which prevent an unintentional displacement of the reaction vessel sliding supports 20, 22.

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* sic; 16?—Trans. Note.

[0041] Each reaction vessel sliding support 20, 22 also has a multiple number of reaction vessel supports 28. The reaction vessel supports 28 extend between the two guide parts 24 and are arranged successively between the connecting parts 26. As can be recognized in particular in Fig. 2, the reaction vessel supports 28 are accommodated on the respective reaction vessel sliding supports 20, 22 in such a way that they can be moved up and down in the direction of an arrow F, which essentially corresponds to the direction of flow. For this purpose, the reaction vessel supports 28 are mounted via elastic elements 30 onto the guide parts 24 and are secured by holding segments 32 of the guide parts 24 so that they will not be detached from guide parts 24. The elastic elements 30 can be formed, for example, by plastic tubing, which can be elastically deformed upon the action of force, due to its elasticity, and the elements expand again upon release and thus prestress the reaction vessel supports 28 in an upward direction in Fig. 2.

[0042] As can also be recognized in the figures, a row 36 of reaction vessels 34 is supported on each reaction vessel support 28 of the reaction vessel sliding supports 20, 22. For this purpose, each reaction vessel support 28 has a multiple number of passage openings 38, wherein the number of passage openings 38 in each reaction vessel support 28 corresponds to the number of reaction vessels 34 in each row 36 of reaction vessels 34. The reaction vessels 34 are inserted into openings 38 in the region of their lower ends in the manner described in detail below and held on the respective reaction vessel supports 28.

[0043] A so-called microtiter plate 40 with a plurality of collecting vessels 42 is disposed in the lowermost positioning plane III. The collecting vessels 42 are disposed in their turn in individual rows, wherein the number of collecting vessels 42 in each row corresponds to the number of reaction vessels 34 in each row and the number of rows of collecting vessels 42 in the microtiter plate 40 corresponds to the number of rows 36 of reaction vessels in the reaction vessel sliding support.

[0044] A collecting tank 44 is arranged under support 12, and this serves for collecting reagents or the like output from reaction vessels 34. The collecting tank 44 is shown by the dashed line in Figs. 1 and 2. Of course, it is possible also to position the collecting tank 44 above the bottom plate 18 between the individual vertical long walls 14.

[0045] In the device 10 according to the invention, a means 46 for introducing and removing reagents is also provided. The means 46 for introducing and removing reagents is formed, for example, by a dispenser tool 46, which is known in and of itself, and which can be moved up and down, on the one hand, in the direction of the arrow F, and which can be moved back and forth, on the other hand, in the direction of arrows P and S in Fig. 1 in the longitudinal direction of support 12.

[0046] The dispenser tool 46 is shown in detail in Figs. 4 and 5. It comprises a body 48, which has a row of reagent output channels 50 as well as a row of pressure output channels 52 on its bottom. The reagent output channels 50 and the pressure output channels 52 are each open toward the bottom of body 48 and extend out from body 48. In addition, a layer of sealing material 54 is provided on the bottom of body 48, in which openings 56 are formed each time in the region of channels 50, 52, and these channels

50, 52 project into or pass through the openings. The number of channels 50, 52 in each row corresponds to the number of reaction vessels 34 in each row 36 of reaction vessels 34. That is, reagents can be introduced simultaneously by the dispenser tool 46 into all reaction vessels 34 of one row 36 through the reagent output channels 50. In addition, all reaction vessels 34 of one row 36 can be pressure-loaded simultaneously via the pressure output channels 52, as will be described in detail below.

[0047] The dispenser tool 46 stands above a pipeline 60 which is connected to a pressure source, e.g., a source of compressed air, so that when a corresponding valve, which is not shown in the figures, is actuated, pressure can be delivered via the pressure output channels 52, into reaction vessels 34. In addition, the dispenser tool 46 stands above a line 58 which is connected to a source for reagents, i.e., reaction solutions or the like. The line 58, for example, can be connected with different fluid sources via an alternating or rotating valve, so that when the valve is opened, the fluid can flow from a specific source via line 58 to the reagent output channels 50 and can be delivered by these into the reaction vessels. Storage tanks for the reagents to be introduced could be stored in a space-saving manner in the lowermost positioning plane, where no microtiter plates or the like are disposed and operation is not adversely affected. The configuration of such fluid sources or the introduction of the fluid to the individual reagent output channels is known in the prior art, so that a detailed description can be omitted here.

[0048] As can be recognized in Fig. 5, the reagent output channels 50 and the pressure output channels 52 can have various lengths and cross-sectional dimensions. The

reagent output channels 50 are made relatively thin and long, while on the other hand, the pressure output channels 52 are made short, so that they do not essentially project beyond the layer of sealing material 54, but have a larger cross section. This has the objective of immersing the reagent output channels 50 which are relatively long relatively far into the individual reaction vessels 34 and thus the reagents come out of the dispenser tool 46 already at a distance from the upper edge of the reaction vessel 34. This contributes to preventing a spilling of reagents into the environment, i.e., into a region outside reaction vessel 34. The special configuration of the pressure output channels 52 is selected such that they make possible the rapid introduction of a large gas volume and a correspondingly rapid generation of pressure due to their relatively large flow cross section upon loading reaction vessel 34 with pressure, which will be described in detail below, but due to their short length make possible the introduction of gas into the reaction vessels close to their upper ends, so that any liquid which has collected in the lower region of the reaction vessel 34 is not flushed out by the entering gas and thus no droplets or aerosols are produced, which could escape from the reaction vessels.

[0049] A first embodiment for reaction vessels 34 of the device according to the invention is shown in Fig. 6. As can be recognized in Fig. 6, the reaction vessels 34 of one row 36 are each joined integrally with one another by web segments 62, so that each row 36 of reaction vessels 34 forms a substantially rigid integral row, which can be displaced into corresponding openings 38 of the reaction vessel support 28. As can be recognized in Fig. 6, the reaction vessels 34 are of conical shape, tapering in the region of the outlet ends 64 of reaction vessels 34, and the openings 38 in the reaction vessel

support 28 are of conical shape, tapering in a corresponding manner, so that the reaction vessels 34 are held centered in the reaction vessel support 28. This is only one type of configuration, however; many other configurations are possible for holding reaction vessels 34 on the reaction vessel support 28. For example, it is possible to provide an edge section of substantially cylindrical form surrounding the outlet ends 64 of reaction vessels 34, which is then inserted into correspondingly shaped openings of the reaction vessel support 38. Further, the reaction vessels 34 can be held onto the reaction vessel support by adhesive or the like.

[0050] The reaction vessels 34 are pointed in shape in the region of their outlet ends 64 similar to a cannula. By these pointed ends, in the course of a transfer of reagents from these vessels into the reaction vessels 34 of a positioning plane disposed thereunder, which will be described below, the reaction vessels 34 can pierce a membrane 70, which is arranged on the upper side of those reaction vessels 34 lying thereunder. A fluid-tight connection for the transfer of reagents between the two positioning planes is created by the tips of the upper row 36 of reaction vessels 34 that penetrate membrane 70 and membrane 70 itself. The consequence of this is that material cannot escape unintentionally from the lower reaction vessels 34 during the transfer of reagents. However, in order to be able to create an equilibration of pressure, a cannula 72 is disposed in each of the reaction vessels 34. If fluid is introduced from the upper reaction vessels 34 into the lower reaction vessels 34, then gas that is expelled from the lower reaction vessels 34 can escape via the cannulas 72 of the upper reaction vessels 34. In order, however, to prevent aerosols from being entrained by the escaping gas, an aerosol filter 74 is arranged in each of cannulas 72, and this filter only allows the

passage of gas, but binds any suspended particles entrained in the gas and thus in turn prevents the suspended particles entrained in the escaping gas from contaminating the environment.

[0051] In addition, a filter 76, which will be described in detail below, is arranged in each of the reaction vessels 34. This filter 76 can have several functions. On the one hand, it serves for the purpose of preventing the undesired passage of fluid through a reaction vessel 34. That is, the passage of fluid will be permitted only if the inside of reaction vessel 34 is loaded with pressure. In addition, however, filter 76 can serve for the purpose of inducing a desired reaction, as will be described later.

[0052] An alternative embodiment of reaction vessels 34' is shown in Fig. 7. The reaction vessels 34' in Fig. 7 are fitted into a corresponding uptake opening 38' of a reaction vessel support 28' (see Fig. 8). The opening 38' is thus formed on an annular support segment 78, which is rigidly joined with the reaction vessel support 28' by wall segments 80. Individual channel segments 82, each of which again provides venting/aeration channels, are formed between the wall segments 80.

[0053] As can be recognized in particular in Fig. 7, the reaction vessel support 28' is formed by two plate parts 84, 86, which are joined together with the intermediate mounting of a layer of aerosol filter 88. The aerosol layer filter 88 is cut out in the region of openings 38', but in the region of the channel-like openings 82, forms a filter in these openings 82, and this filter retains suspended particles entrained in the gas when gas escapes from the lower reaction vessels 34'.

[0054] A layer of sealing material 90, which has a corresponding opening 92 in the region of openings 38' and channels 82, is in turn disposed on the bottom of the reaction vessel support 28'. By lowering the reaction vessel support 28', which will be described in detail below, the layer of sealing material is applied to the lower reaction vessel support 34' and forms a fluid-tight connection with the latter. By introducing fluid from the upper reaction vessels 34' into the lower reaction vessels 34', expelled gas can escape through the channels 82 via the filter 88.

[0055] It is possible also in the embodiment according to Fig. 7 to provide membranes that prevent an unintentional escape of aerosols or the like on the upper side of the reaction vessels 34'. In this case, the lower ends of reaction vessels 34' must in turn be pointed, and the membranes must be comprised of a material which is permeable to gas, but retains aerosols or the like. The use of such a membrane material is also conceivable in the embodiment according to Fig. 6; if the membrane material is permeable to gas, then for example, cannulas 72 in the individual reaction vessels 34 could be dispensed with, since the gas escapes away from the lower reaction vessels 34 through the membrane. Providing membranes on the upper ends of the reaction vessels has the advantage that a contamination of the reaction vessel support of the upper reaction vessels can be avoided also when layers of sealing material are used for a tight seal relative to the environment.

[0056] The principal mode of operation of the device 10 according to the invention will be described below. A reaction agent, i.e., reagents, are first introduced by the dispenser tool 46 into the reaction vessels 34 of the reaction vessel sliding support 20 in

positioning plane I. This is conducted in such a way that the dispenser tool 46 shown in Fig. 1 is moved first in the direction of an arrow S over a row 36 of reaction vessels 34 in positioning plane I. If the dispenser tool 46 lies above such a row 36, then it is lowered in the direction of arrow F, until, by its layer of sealing material 54, it bumps into the upper end of reaction vessels 34 and thus produces a fluid-tight connection, as can be seen, for example, also with reference to Fig. 7. Alternatively, however, it is also possible that the reagent output channels 50 of the dispenser tool 46 are pointed in shape at their lower ends, so that they can penetrate a membrane disposed at the upper ends of the reaction vessels, as is shown in Fig. 6 and thus create the fluid-tight connection. The same thing applies to the pressure output channels 52.

[0057] After lowering the dispenser tool 46 onto the reaction vessels 34, a desired reaction agent is introduced into the reaction vessels 34 of one row 36 in positioning plane I via the reagent output channels 50. When this process has ended, the dispenser tool 46 is again removed and further moved stepwise to the next row 36 in positioning plane I. This process is repeated until all reaction vessels 34, i.e., all reaction vessels 34 provided for a specific reaction are filled with the desired reaction agent each time in positioning plane I. For this purpose, it is of course also possible that the dispenser tool 46 has several rows of reagent output channels 50 disposed one behind the other and corresponding rows of pressure output channels 52, so that simultaneously several rows 36 of reaction vessels 34 can be filled.

[0058] Now, if a fluid is to be transferred from reaction vessels 34 in positioning plane I to reaction vessels 34 in positioning plane II, then first the reaction vessel sliding

support 22 in positioning plane II is moved into positioning region b. This is carried out by moving the dispenser tool 46 in the direction of an arrow P over the reaction vessel sliding support 22 and then lowering it in the direction of the arrow F, until it is placed on the reaction vessels 34 of the positioning plane II and then is moved back again in the direction of arrow S and thus takes along the reaction vessel sliding support 22. The reaction vessel sliding support 22 is thus moved into the positioning region b. In a corresponding manner, the reaction vessel sliding support 20 is subsequently moved by the dispenser tool 46 from the positioning region c into the positioning region b. In the representation of Fig. 1, the positioning region b thus forms a transfer positioning region I, in which the reaction vessels 34 of positioning plane I lie above the reaction vessels 34 of positioning plane II. In particular, in the embodiment shown, a 1 to 1 allocation of reaction vessels is encountered, i.e., a row 36 of reaction vessels of positioning plane II with a corresponding number of reaction vessels 34 is provided for each row 36 of reaction vessels of positioning plane I.

[0059] In order to transfer liquid from the reaction vessels of positioning plane I into the reaction vessels of positioning plane II, the dispenser tool 46 is again disposed over a row 36 of reaction vessels of positioning plane I and is lowered in the direction of the arrow F, until it is placed in turn on reaction vessels 34. The dispenser tool is then further lowered, however, until it is moved into a position shown in the left half of Fig. 2. In this position the dispenser tool 46 presses the reaction vessels 34 down against the prestressing force of the elastic elements 30. Depending on the configuration of the reaction vessels or the reaction vessel support, either a pointed end 64 of the reaction vessel 34 is now immersed in the reaction vessels 34 lying thereunder, thus penetrating

membrane 70 (Fig. 6), or the layer of sealing material 90 of the reaction vessel support 28' (Fig. 7) comes to lie on the upper side of reaction vessels 34' of positioning plane II, so that in each case a fluid-tight connection between the reaction vessels 34 or 34' of the two positioning planes I and II is created. The reaction vessels 34 joined with the web segment 62 in each row of reaction vessels provide a particularly stable arrangement of the reaction vessels, which in particular assures a reliable operation of the device according to the invention when pressure is exercised by means of the dispenser tool.

[0060] It should be mentioned here, however, that the production of such a fluid-tight connection is not absolutely necessary; in particular, it may not be required for various reactions. Instead of this, it is possible to form the reaction vessels as shown in Fig. 2 so that they are immersed by an output segment into the reaction vessels lying thereunder without forming a fluid-tight seal, and inject the liquid into these at a distance down from the upper edge of the reaction vessels of the lower positioning plane, so that also the unintentional spilling of reagents into the environment can be extensively suppressed.

[0061] In order to transfer fluid or liquid between the two positioning planes, in the lowered state of the dispenser tool 46 shown at the left in Fig. 2, an increased air pressure is now produced via the pressure output channels 50 into the individual reaction vessels of positioning plane I, so that fluid contained in these reaction vessels is pushed through the filter 76 and thus is delivered to the reaction vessels lying thereunder. After terminating this transfer, the dispenser tool 46 is again raised, moved

to above the next row 36 of reaction vessels 34 in positioning plane I, lowered again in the direction of the arrow F and the process of pressure transfer is repeated. If the liquid is released from all rows 36 in positioning plane I, then, as has already been described previously, the reaction vessel sliding support 20 of positioning plane I will be moved back again into the positioning region c, so that now the reaction vessel sliding support 22 of positioning plane II is freely accessible to the dispenser tool 46 from the top and for example, as previously described, can be moved again into the positioning region a by means of the dispenser tool 46. In this state, a reaction agent can then be introduced again into the reaction vessels 34 of the reaction vessel sliding support 22 by means of the dispenser tool 46, in order to again conduct a reaction, or the introduction can be carried out by an appropriate pressure loading, as it has been described above for transferring reagents between positioning planes I and II, in order to transfer liquid contained in the reaction vessels 34 of the reaction vessel sliding support 22 into the collecting vessels 42 of the microtiter plate 40. Positioning plane III thus forms a collecting level, in which the reaction products of the last reaction step are collected in microtiter plate 40 and are ready for the subsequent analysis, etc. It should be mentioned here that the microtiter plate 40 could likewise be disposed in positioning region b in positioning plane III. Then a shifting of the reaction vessel support 22 between positioning regions a and b would not be necessary for the different reactions.

[0062] The elastic elements 30 can also be designed in such a way that they actively cause the displacement of the reaction vessel support 28 in direction F. For example, it can be provided that the elastic elements 30 are designed as flexible tubing and are connected to a vacuum pump, so that when the tubing-like elements 30 are evacuated,

they contract and thus bring the reaction vessel support 28 into the position shown at the top left in Fig. 2.

[0063] It is also possible with the device 10 according to the invention to release byproducts or waste products, which may form in the different reaction steps, into the collecting tank 44 and not into reaction vessels lying thereunder. This release can be induced in a corresponding manner by pressure loading the reaction vessels by means of the dispenser tool 46, wherein, however, the corresponding reaction vessels or the reaction vessel sliding support bearing these are/is to be positioned such that during the pressure loading and the fluid release produced thereby, the liquid 2 can drip into the collecting tank 44 without falling onto a reaction vessel sliding support arranged thereunder. It is particularly advantageous if the reaction vessels are formed in such a way that they support membranes at their upper ends (see Fig. 6), since, if reagents drip out of another reaction vessel sliding support arranged on top, an unintentional introduction of these reagents into the reaction vessels of another reaction vessel sliding support arranged below is prevented. Such membranes also prevent any unintentional contamination of the inner space of the corresponding reaction vessels.

[0064] It is also possible with the device 10 according to the invention to remove reaction agent from reaction vessels of any positioning plane by means of the dispenser tool 46 or an appropriately designed tool and to transfer it into the reaction vessels of another positioning plane. It is also possible to design the number of reaction vessels in the different positioning planes in different ways. Thus, for example, depending on the type of reaction each time, only a single row 36 of reaction vessels 34 is provided in

positioning plane I, and these are then moved stepwise over the reaction vessel sliding support 22 of positioning plane II, i.e., the rows 36 of reaction vessels supported in this latter, in order to transfer liquid in the manner described previously. An important feature, however, is the fact that individual reaction channels are made ready for the processing of individual reagents by the different positioning planes, so that the danger described above with reference to the prior art of the leakage of reaction products of one reaction channel into an adjacent reaction channel can be avoided.

[0065] Reference is also made here to the fact that the above-described transfer of pressure between the individual positioning planes need not necessarily be produced by loading with a gas pressure, but rather it is also possible to produce an overpressure in the individual reaction vessels by an appropriate pressure input from reagents, i.e., liquid reagents, which leads to the elimination of filter 76 and to the corresponding output of reagents, i.e., liquid. It is also possible to produce the transfer by another action. Thus, for example, the transfer can also be driven by electrical or magnetic fields and can be carried out in any direction, i.e., it can be carried out from top to bottom and from bottom to top. Filters 76 can also be designed in such a way that the gravitation action alone effects a transfer. This is possible, for example, with a correspondingly porous and thick configuration of filters 76, so that a liquid requires a prespecified time period in order to penetrate the respective filter.

[0066] It can also be provided in the device according to the invention that by means of lowering the dispenser tool 46 onto the reaction vessels 34 of positioning plane I, on the one hand, these reaction vessels with the allocated reaction vessel support 28 are

lowered, and on the other hand, simultaneously, reaction vessels that are disposed directly thereunder in positioning plane II are also lowered. This can be accomplished, for example by making the lifting region of the reaction vessel support 28 in positioning plane I at least twice the size of this region in the reaction vessel support in positioning plane II. If the reaction vessels in positioning plane II are then lowered, the reaction vessel support 28 [of plane I] is applied to the reaction vessels of positioning plane II lying thereunder, but moves further and thus moves downward the reaction vessels lying thereunder together with the reaction vessel support belonging thereto, so that these are immersed in a corresponding manner in the reaction vessels or collecting vessels of positioning plane III.

[0067] The filters can comprise, for example, filters made up of several layers or they can comprise multi-layer or single-layer fiberglass filters. The selection of the filter depends each time on the type of reaction that is to be conducted in a specific reaction vessel, i.e., in a specific positioning plane.

[0068] It should be pointed out that the number of reaction vessels in each positioning plane or each row can be adapted to the particular requirements. Therefore, it is possible that only a single reaction vessel can be disposed in each positioning plane or each row, which is then adapted in its size to the desired reaction yield.

[0069] A schematic diagram of a device 10 according to the invention, which comprises five positioning planes I-V, is shown in Fig. 9. Each of positioning planes I-V has two positioning regions A, B. Each positioning region B in the different positioning planes 10 thus forms an uptake positioning region, while in contrast, each positioning region A

forms an output positioning region. As can be recognized in Fig. 9, under each output positioning region A of a positioning plane, there is arranged an uptake positioning region B of the positioning plane lying thereunder. There results a step-like arrangement of the positioning regions of the different positioning planes, in which the output positioning regions of the different positioning planes are then each freely accessible from the top, in order to be able to introduce reagents or pressure into the reaction vessels disposed in each positioning plane I-IV by means of the dispenser tool 46 in the manner described previously and to be able to freely move the reaction vessel sliding supports into the individual positioning planes I-IV by means of the dispenser tool 46.

[0070] The positioning regions A and B directly following one another of successive positioning planes each form a transfer positioning region T, in which reagents can be transferred between the reaction vessels in these positioning planes and positioning regions. As is indicated also in Fig. 9, it is possible to use the output positioning region A also as uptake positioning region B in positioning plane I, i.e., to position the dispenser tool 46 for introducing reagents into the reaction vessels of positioning plane I over the positioning region A or (B). In a corresponding manner, in positioning plane IV, the uptake positioning region B or (A) can also serve as the output positioning region for delivery into the reaction vessels or collecting vessels of positioning plane V.

That is, in this case, the positioning plane V has two uptake positioning regions B.

[0071] In the representation according to Fig. 9, the individual positioning regions A and B are shown in such a way that they each serve either for positioning a multiple number of rows of reaction vessels or provide the positioning of individual rows of reaction

vessels. That is, Fig. 9 can be considered in such a way that it reproduces the case of the minimum number of rows of reaction vessels, i.e., at least two positioning regions must be provided for each row of reaction vessels in each positioning plane. It must also be provided that the reaction vessels of one positioning plane can be positioned in such a way that at least one row of reaction vessels of the positioning plane or planes lying thereunder is exposed to free access by dispenser tool 46, in order to be able to operate or displace the reaction vessels of the positioning plane or planes lying thereunder by means of the dispenser tool 46.

[0072] The application of the device according to the invention, as it is shown in Figs. 1 and 2, is described below for isolating plasmid DNA from bacteria. In this process, bacteria pellets are first treated with suitable solvent at a position outside device 10, so that a complete lysis of these samples occurs. After completion of lysis and suitable pretreatment, these reaction batches are transferred to reaction vessels 34 of positioning plane I. Filters 76 are placed in these reaction vessels made of a polypropylene filter material comprised of three layers with decreasing pore size. That is, the uppermost filter layer has a pore size of 210 μm, the intermediate filter layer has a pore size of 80 μm and the lowermost filter layer has a pore size of 40 μm. In such filters, when the liquid is first introduced into reaction vessels 34 of positioning plane I, it begins to penetrate filter 76, but the capillary movement is stopped due to the decrease in pore size, so that the liquid cannot completely penetrate this filter. The use of such filters leads to the fact that flakes or gelatinous material contained in the lysed bacterial material are filtered out. In addition, it has been shown that the use of such filters even

promotes the breaking up of such materials, which leads to a clearly better and easier filtration being carried out.

[0073] In order to transfer the liquid contained in the reaction vessels 34 of positioning plane I into the reaction vessels 34 of positioning plane II, i.e., for the above-described filtration, the reaction vessel sliding support 20 of positioning plane I is shifted into positioning region b, which is an output positioning region for reaction vessel sliding support 20. The reaction vessel sliding support 22 in positioning plane II has also already been previously shifted into the positioning region b, which forms an uptake positioning region for this reaction vessel sliding support 22. By applying a pressure by means of dispenser tool 46, in the manner described above, the lysed bacterial material contained in the reaction vessels 34 in positioning plane I is filtered through filters 76 and the filtered liquid is collected in the reaction vessels 34 of positioning plane II.

[0074] In the reaction vessels 34 of positioning plane II, the material used for filters 76 is a fiberglass filter material, on which the DNA material deposits in a way known in and of itself. The liquid contained in reaction vessels 34 of positioning plane II is no longer necessary and thus forms waste material. This is discharged by application of pressure on the reaction vessels of this positioning plane through filters 76 in this positioning plane into collecting tank 44 for the reaction vessel sliding support 22 disposed in positioning region b. Subsequently a purification step is conducted by first introducing a 70-80 % ethanol solution via dispenser tool 46 into the reaction vessels 34 of positioning plane II, and then discharging it into collecting tank 44 by application of pressure. The filter material with the DNA material deposited thereon is then dried by

application of compressed air. Two such purifying and drying cycles are run each time before the next series of samples. This leads to a longer drying time, without the need for interrupting the processing process.

[0075] After drying, the reaction vessel sliding support 22 in the positioning plane II is moved into the positioning region a, so that the reaction vessels 34 thereof are arranged each time over the collecting vessels 42 of microtiter plate 40 in positioning plane III. Then the DNA material deposited on filter material 76 of positioning plane II is eluted by introduction of a solvent, for example, water. The DNA material is stripped from the filters by this solvent and can then be discharged together with the solvent into the collecting vessels 42 in positioning plane III by applying pressure by means of dispenser tool 46. Then the isolated DNA material which can be used for further investigation is contained in these collecting vessels 42.

[0076] With the above-described device according to the invention, it is possible to conduct a plurality of the most varied chemical or biochemical reactions. In particular, the parallel conducting of a plurality of reactions is possible in individual reaction channels each time. Depending on the selection of the number of reaction vessels or rows of reaction vessels each time, the number of individual reaction channels can be adapted to the desired requirements. A plurality of different transfer possibilities for reagents between different positioning planes is offered by the mobility of the reaction vessels in the individual positioning planes between different positioning regions. Therefore, even with a large number of reaction sequences to be conducted in parallel,

the time required for these reactions can be clearly reduced, even in multistage reactions, by the device according to the invention.

[0077] Due to the stacked arrangement of the different positioning planes, the space needed in a laboratory for the device according to the invention is very small. In addition, due to the special configuration of the device according to the invention, a fully automatic conducting of reaction sequences is possible without the intervention of operating personnel. The fluid-tight connection between reaction vessels of different positioning planes or between the means for introducing and removing reagents and the reaction vessels, which can be achieved in various ways, provides a protection from contamination, so that the discharge of reagents into the environment, which could lead to adversely affecting the reactions of adjacent reaction channels is avoided.

[0078] The number of positioning planes or positioning regions can be adapted to the different reaction requirements each time in the desired manner, so that reactions with any number of reaction steps can be conducted. It is possible with the device according to the invention to conduct reactions not only in a sequence from top to bottom, for example, but also, by suitable selection of the means for introducing and removing reagents or of the individual reaction vessels, to be able to transfer liquid from reaction vessels arranged further down into reaction vessels arranged further up.

Patent claims

1. A device (10) for conducting chemical reaction sequences, comprising:

--a support (12) with a multiple number of positioning planes (I-III), which are arranged successively in the direction of flow (F) and are substantially parallel to one another, wherein each positioning plane (I-III) comprises a multiple number of positioning regions (a, b, c) lying next to one another substantially orthogonal to the direction of flow (F), and wherein, relative to at least one positioning region (a, b, c) in one of the positioning planes (I-III), there is another positioning region (a, b, c) aligned in the direction of flow (F) to the first region in at least one directly adjacent positioning plane (I-III),

--in at least one of the positioning planes (I, II, III) at least one reaction vessel sliding support (20, 22) with at least one reaction vessel (34), wherein the reaction vessel sliding support (20, 22) can be moved in the assigned positioning plane (I, II), so that the at least one reaction vessel (34) or at least some of the reaction vessels (34) supported on the reaction vessel sliding support (20, 22) can be arranged in at least one transfer positioning region (T), wherein a reaction vessel of a directly adjacent positioning plane (I, II, III) can be assigned to each reaction vessel (34) arranged in the at least one transfer positioning region (T) for the selective transfer of reagents between these reaction vessels (34).

2. The device according to claim 1, further characterized in that the at least one reaction vessel sliding support (20, 22) bears at least one row (36) of reaction vessels (34), in which at least one reaction vessel is disposed.

3. The device according to claim 2, further characterized in that the at least one row (36) of reaction vessels (34) is supported on the at least one reaction vessel sliding support (20, 22) by a reaction vessel support (28) assigned to this row (36).

4. The device according to one of claims 1 to 3, further characterized in that each reaction vessel (34) borne on the at least one reaction vessel sliding support (20, 22), for the transfer of reagents between this vessel and a respectively assigned reaction vessel (34) in a directly adjacent positioning plane (II, III) in the direction of flow (F), can be moved onto the assigned reaction vessel (34) of the directly adjacent positioning plane (II, III).

5. The device according to claim 3 and claim 4, further characterized in that the reaction vessel support (28) bearing the at least one row (36) of reaction vessels (34) is arranged so that it can be moved up and down on the at least one reaction vessel sliding support (20, 22) in the direction of flow (F).

6. The device according to claim 5, further comprising movement means (46) for executing the up-and-down movement of the reaction vessel support (28).

7. The device according to claim 6, further characterized in that the movement means (46) are designed for exercising a pressure force on each reaction vessel (34) borne on the reaction vessel support (28), wherein, when exercising the pressure force, each reaction vessel (34) can be moved with the reaction vessel support (28) against a

prestressing force onto the assigned reaction vessel (34) of the directly adjacent positioning plane (II, III).

8. The device according to claim 7, further characterized in that the prestressing force is produced by prestressing means (30) acting between the at least one reaction vessel sliding support (20, 22) and the reaction vessel support (28), preferably spring means, elastically deformable plastic elements (30) or the like.

9. The device according to claim 6, further characterized in that the movement means comprise displacement means acting between the at least one reaction vessel sliding support (20, 22) and the reaction vessel support (28).

10. The device according to one of claims 4 to 9, further characterized in that sealing means (64, 70; 90) are provided, which, in a state where the reaction vessels (34; 34') of two directly adjacent positioning planes are moved toward one another, produce a substantially fluid-tight seal between the reaction vessels (34; 34') of the different positioning planes assigned to one another each time.

11. The device according to claim 10, further characterized in that the sealing means (64, 70) comprise an essentially point-shaped outlet end (64) of the at least one reaction vessel (34) of a positioning plane as well as a receiving end sealed by membrane means (70) of the respectively assigned reaction vessel (34) of the other positioning plane, wherein, when the reaction vessels (34) of the different positioning planes on opposite sides approach one another, the membrane means (70) can be penetrated by the pointed outlet ends (64) and form a fluid-tight seal with these ends.

12. The device according to claim 5 and claim 10, further characterized in that the sealing means (90) comprise a layer of sealing material (90) on one side of the reaction vessel support (28'), which is turned toward the assigned reaction vessels (34') of the directly adjacent positioning plane, wherein when the reaction vessel support (28') moves onto the reaction vessels (34') of the directly adjacent positioning plane, the sealing material layer (90) is applied to the receiving end of the reaction vessels (34') of the directly adjacent positioning plane and forms with it a fluid-tight seal.

13. The device according to one of claims 10 to 12, further comprising venting means (72; 82), which make possible an aeration or venting of the reaction vessels (34; 34') with the fluid-tight connection of the reaction vessels (34; 34') of two directly adjacent positioning planes.

14. The device according to claim 13, further characterized in that the venting means (72) comprise venting channel means (72), which extend away from the outlet ends (64) of the reaction vessels (34), preferably within the respective reaction vessels (34), and preferably are open to the environment via filtering means (74).

15. The device according to claim 12 and claim 13, further characterized in that the at least one reaction vessel (34') on the assigned reaction vessel support (28') is supported in the region of its outlet end, and that the venting means (82) provided on the reaction vessel support (28'), passing through the support and the layer of sealing material (90) approximately in the direction of flow (F) and the outlet end of the at least

one reaction vessel (34') comprise surrounding venting channel means (82), which, upon application of the reaction vessel support (28') on the receiving end of the respective assigned reaction vessel (34') of the directly adjacent positioning plane, produce a connection for the flow of gas between the inside space of the assigned reaction vessel (34') of the directly adjacent positioning plane and the environment, preferably via filter means (88).

16. The device according to one of the preceding claims, further comprising sealing means (76), preferably filter means (76), in the at least one reaction vessel (34), preferably in the region of the outlet end (64), which sealing means (76) make possible a passage of fluid only upon an external action.

17. The device according to claim 16, further characterized in that the external action can result by application of a pressure or of an underpressure on the inside of the reaction vessels (34), or can be produced by electrical, magnetic or gravitational actions.

18. The device according to one of the preceding claims, further comprising means for introducing and removing reagents (46) for introducing reagents into the at least one reaction vessel (34) in at least one of the positioning planes (I-III) or for removing reagents from the at least one reaction vessel (34) of at least one of the positioning planes (I-III).

19. The device according to claim 18, further characterized in that the means for introducing and removing reagents (46) can be joined with the respective reaction vessels (34) in a fluid-tight manner (at 54) for introducing and removing reagents.

20. The device according to claim 18 or 19, further characterized in that each positioning plane (I-V) comprises at least one introduction/removal positioning region (A), wherein during the positioning of at least some of the reaction vessels provided in one positioning plane (I-V) in the at least one introduction/removal positioning region (A), these reaction vessels are freely accessible from one side to the means for introducing and removing reagents (46), for introducing reagents into these vessels and removing them therefrom in the direction of flow (F), preferably from an upper side.

21. The device according to claim 7 and one of claims 18 to 20, further characterized in that the means for introducing and removing reagents (46) form movement means (46).

22. The device according to one of the preceding claims, further characterized in that the reaction vessel sliding supports (20, 22) can be moved linearly in the respectively assigned positioning planes (I-III).

23. The device according to one of claims 1 to 21, further characterized in that the reaction vessel sliding supports in the respective positioning planes can be moved on approximately circular tracks.

24. The device according to one of the preceding claims, further comprising means (46) for effecting the movement of the reaction vessel sliding supports in the assigned positioning planes.

25. The device according to claim 18 and according to claim 24 and if desired, according to another of the preceding claims, further characterized in that

the means for introducing and removing reagents (46) form the means (46) for effecting the movement of the reaction vessel sliding supports in the assigned positioning planes.

26. The device according to one of the preceding claims, further characterized in that the at least one reaction vessel (42) in one of the positioning planes (III), preferably of the last positioning plane (III) in the direction of flow, is a collecting vessel (42) for the uptake of the reaction products produced by the chemical reaction.

27. The device according to one of the preceding claims, further comprising collecting tank means (44) subsequent to the last positioning plane (III) in the direction of flow.

28. The device according to one of the preceding claims, further characterized in that at least some of the positioning planes (I-V) comprise an uptake positioning region (B) and an output positioning region (A), that the uptake positioning region (B) of such a positioning plane (I-V) in the direction of flow is aligned with the output positioning region (A) of a preceding positioning plane (I-IV) in the direction of flow (F), and/or that the output positioning region (A) of such a positioning plane (I-IV) is aligned in the direction of flow (F) with the uptake positioning region (B) of a following positioning plane (II-V) in the direction of flow (F).

29. The device according to claim 28, further characterized in that at least the first positioning plane (I) in the direction of flow (F) comprises an uptake/output positioning region (A), (B), which forms both the uptake positioning region (B) as well as also the output positioning region (A) .

30. The device according to claim 28 or 29, further characterized in that

the last positioning plane (V) in the direction of flow (F) comprises only uptake positioning regions (B), preferably one uptake positioning region (B).

31. The device according to one of claims 28 to 30, further characterized in that the positioning regions (A, B) of the different positioning planes (I-II) are arranged in such a way that the reaction vessel sliding supports in each positioning plane (I-V) can be arranged relative to their respective positioning planes (I-V) such that each reaction vessel sliding support can be arranged in any other positioning plane, preferably by means (46) for introducing and removing reagents, with its (their) allocated reaction vessel(s) in each of the positioning regions (A, B) provided for these reaction vessels.

32. The device according to claim 31, further characterized in that the uptake and output positioning regions (B, A) of the different positioning planes (I-V) are disposed in step-like structure, wherein at least one part of each output positioning region (A) is not covered by a positioning region (A, B) of a preceding positioning plane (I-IV) in the direction of flow (F).

33. A method for conducting chemical reaction sequences, in particular with a device according to one of the preceding claims, comprising the following steps:

a) Introducing reagents into the at least one reaction vessel (34) of a first positioning plane (I),

b) Conducting a chemical reaction, an adsorption reaction, an adsorption reaction of a substance mixture or the like, in the at least one reaction vessel (34),

c) Arranging the at least one reaction vessel (34) of the first positioning plane (I) and the reaction vessel (34) allocated each time of a second positioning plane (II) directly following the first positioning plane (I) in a transfer positioning region (T) of the two positioning planes (I, II),

d) controlled transferring of at least one part of the reaction products obtained in step b) into each allocated reaction vessel (34) of the second positioning plane (II), wherein the at least one reaction vessel (34) of the first positioning plane (I) or/and the reaction vessel (34) of the second positioning plane (II) respectively assigned each time can be positioned in such a way that the at least one reaction vessel (34) in the second positioning plane (II) is freely accessible for the introduction of reagents into it via the means (46) for introducing and removing reagents or/and is positioned for the controlled transfer of reaction products contained in it into a respectively assigned reaction vessel (42) of a third positioning plane (III) which follows the second positioning plane (II).

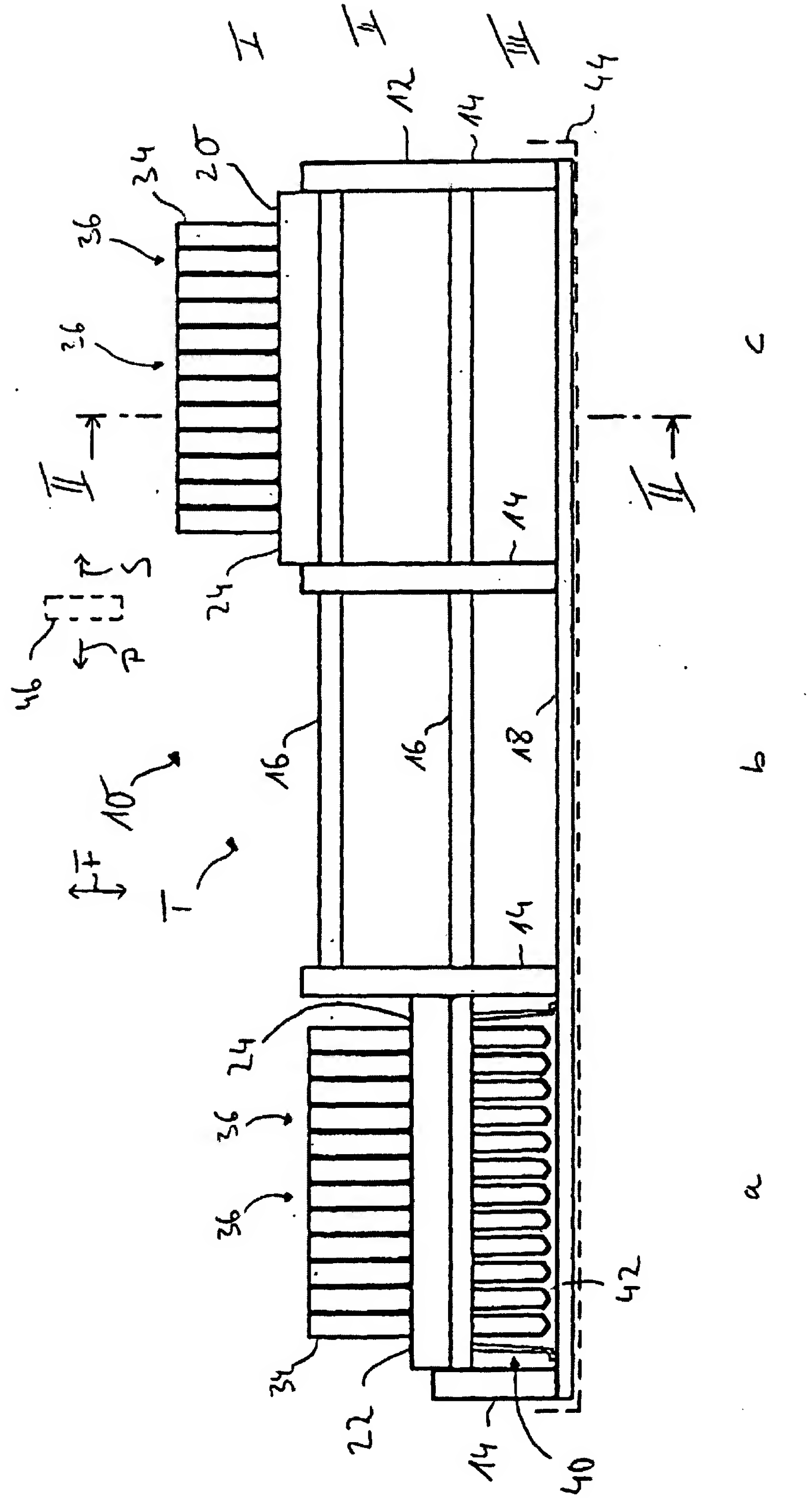

Fig. 1

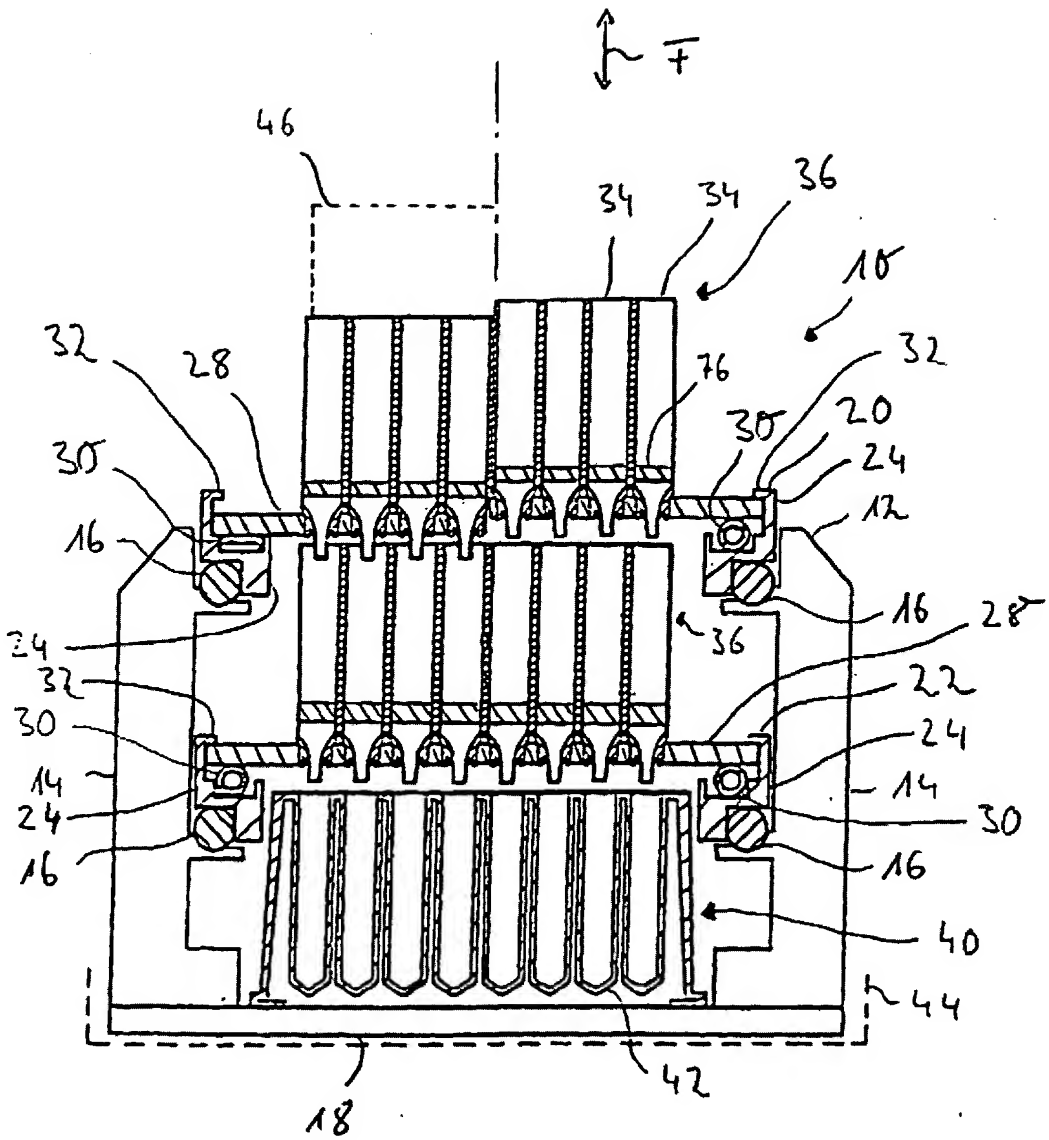
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Fig. 2

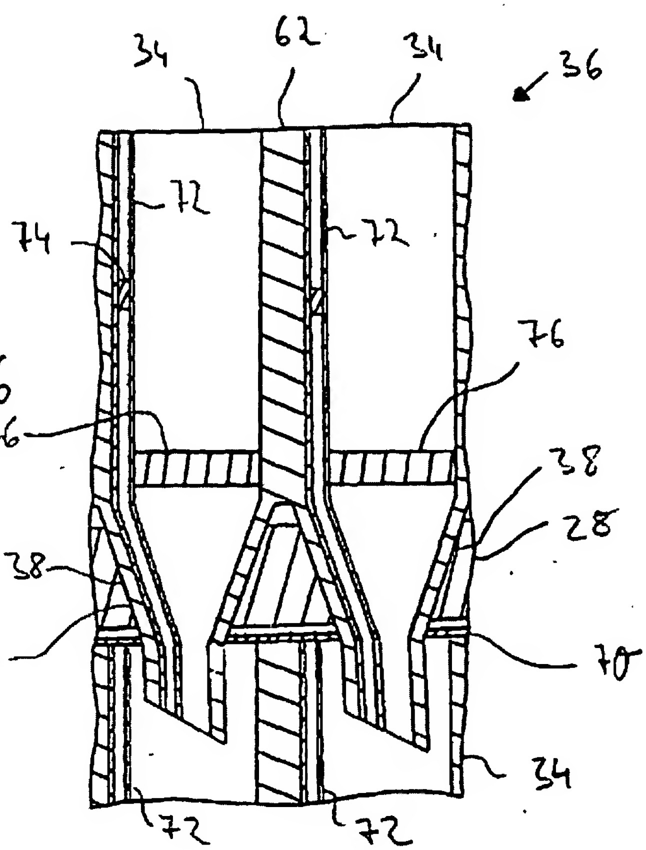
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Fig. 6

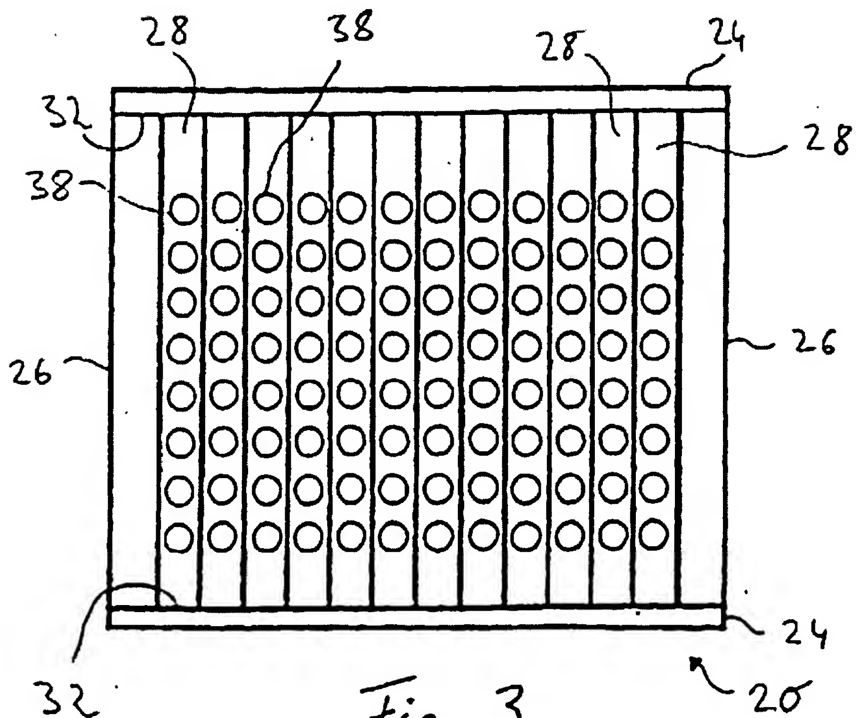
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Fig. 3

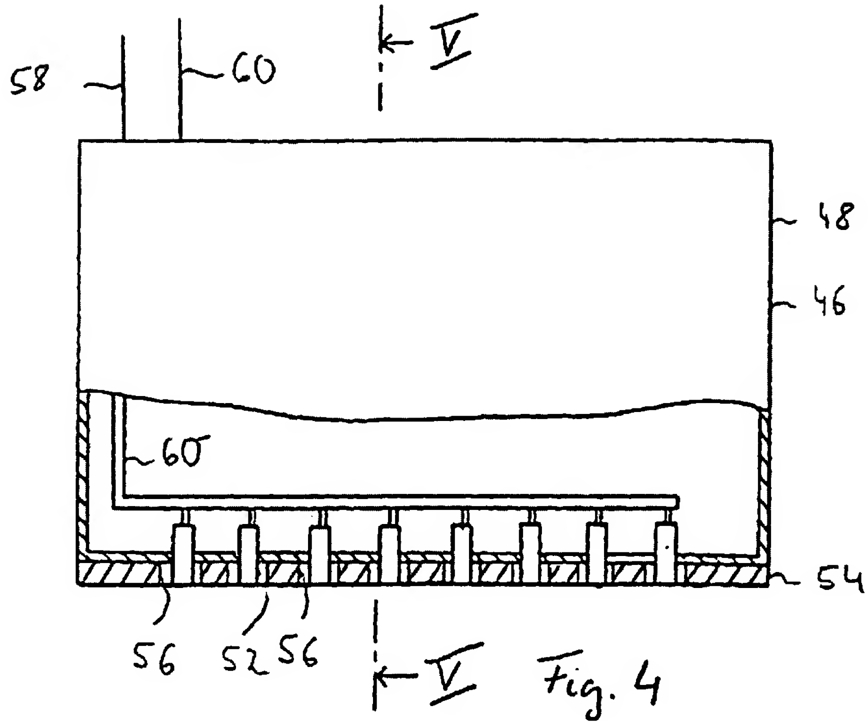

Fig. 4

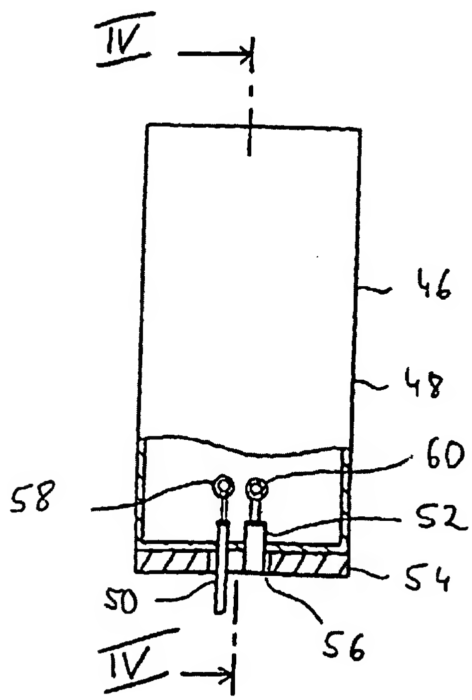

Fig. 5

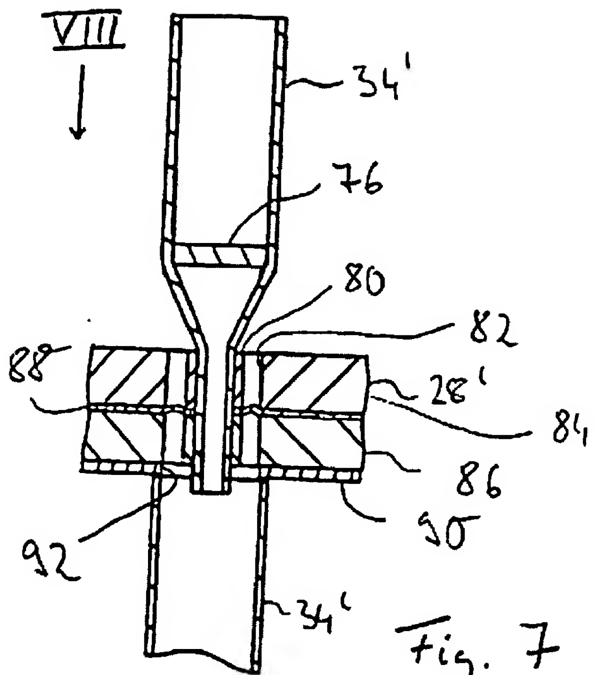

Fig. 7

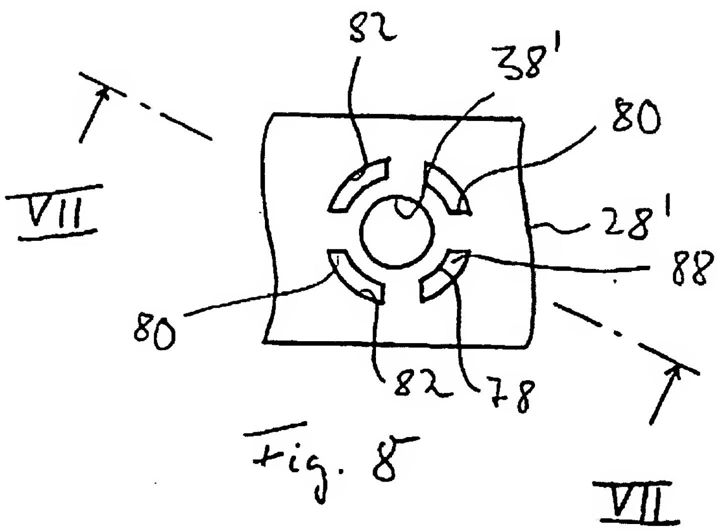

Fig. 8

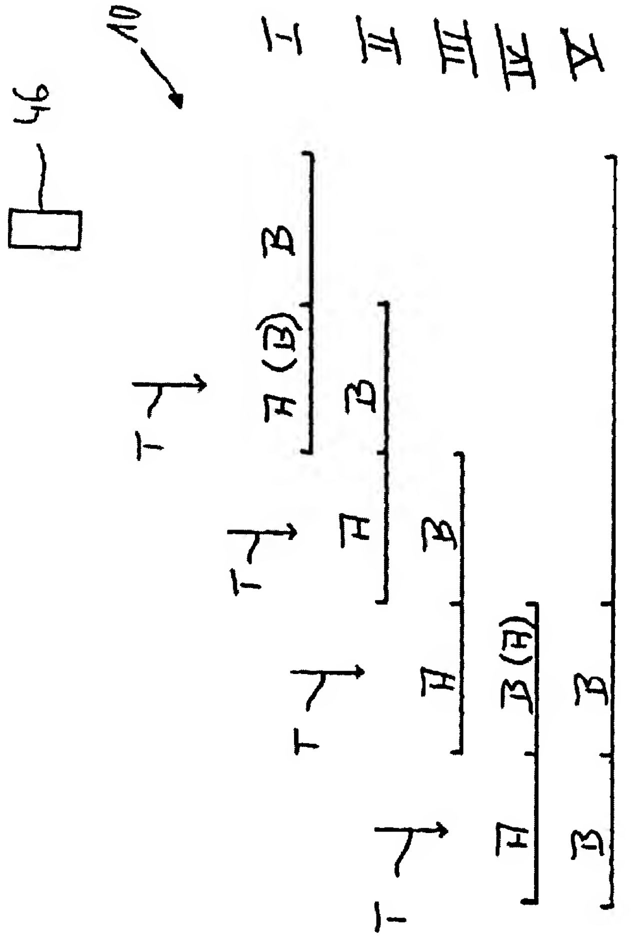

Fig. 9

EP 0 925,828 A1

European Patent Office

EUROPEAN SEARCH REPORT

Number of the Application
EP 97 12 2306

DOCUMENTS CONSIDERED PERTINENT

Category	Citation of the document, with indication, if necessary of the pertinent parts	Claim concerned	Classification of the application examined (Int. Cl.6)
X	US 5,645,723 A (MASATOSHI FUJISHIRO ET AL.) July 8, 1997	1, 2, 4-9 16-18 20-22, 24, 26-33	B01J19/00 B01L3/00 //CN12N15/10
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A	DE 196 05 814 A (INNOVA GMBH) August 21, 1997 *entire document*	1-33	
A	WO 89 10188 A (EUROPAISCHES LABORATORIUM FUR MOLEKULARBIOLOGIE (EMBL) November 2, 1989 *entire document*	1-33	
A	US 5,538,849 A (HIROAKI UEMATSU ET AL.) July 23, 1996 *Abstract; Figures*		
A	EP 0 248,690 A (CLONATEC) December 9, 1987 *Abstract;Figures*		
A	US 4,948,564 A (DAVID ROOT & GEORGE LYMAN) August 14, 1990 *Abstract; Figures*		

Technical fields searched (Int. Cl. 6)
B01J
B01L
G01N
C12N

The present search report was prepared for all patent claims.

Place of Search	Date of search completion	Searcher
The Hague	May 28, 1998	Stevnsborg, N

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X: particularly pertinent alone
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